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EXAMINER

WILSON, MICHAEL C

ART UNIT	PAPER NUMBER
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1632

IS

DATE MAILED: 08/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/786,817

Applicant(s)

SMITH ET AL.

Examiner

Michael C. Wilson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1) ☒ Responsive to communication(s) filed on 04 June 2003.

2a) ☐ This action is FINAL.

2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

4) ☒ Claim(s) 12, 14-21, 25-28, 30-39, 43, 44 and 46-50 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.

6) ☒ Claim(s) 12, 14-21, 25-28, 30-39, 43, 44 and 46-50 is/are rejected.

7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.

8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some \* c) ☒ None of:

1. ☒ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 12.

4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other:

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election of Group II, claims 12, 14-21, 25-28, 30-39, 43, 44 and 46-50, in Paper No. 14 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 12, 14-21, 25-28, 30-39, 43, 44 and 46-50 are pending and under consideration in the instant application.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

### ***Priority***

Acknowledgment is made of applicant's claim for foreign priority to PCT/GB99/03031, filed on 9-13-99, now WO00/15764 and 9819912.8 filed in the United Kingdom on 9-11-98. It is noted, however, that applicant has not filed a certified copy of the applications as required by 35 U.S.C. 119(b). A copy of WO00/15764 has been placed in the file.

### ***Drawings***

The specification describes Figures 1-8 (pg 13, line 24), but no drawings are present in the application.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12, 14-21, 25-28, 30-39, 43, 44 and 46-50 are rejected under 35 U.S.C.

112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed toward culturing ES cells in the presence of a compound that promotes propagation of ES cells and a compound that inhibits MEK. The claims are being examined as they relate to culturing ES cells in the presence of a compound that promotes propagation of ES cells and PD098059.

The specification teaches D027 ES cells which are lif<sup>-/-</sup> and have an IRES- $\beta$ -geo reporter gene inserted within the oct-4 gene locus. The structure or function of the "IRES- $\beta$ -geo reporter gene inserted within the oct-4 gene locus" cannot be envisioned; it is unclear if the reporter protein is expressed under the control of the oct-4 promoter or if the IRES- $\beta$ -geo reporter gene replaces the oct-4 gene. The specification teaches ZIN40 ES cells which express  $\beta$ -gal in differentiated cells. The structure or function of the ZIN40 cells cannot be determined; it is unclear if  $\beta$ -gal is expressed in all cells that undergo any amount of differentiation or only certain types of differentiation; it cannot be determined how to regulate expression of a protein so that it is expressed upon cell

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differentiation. D027 cells were used in a self-renewal assay where PD098059 was added to the cells (pg 18, line 4-14). The results indicated PD098059 increased self-renewal at a concentration of 2-25  $\mu$ M but not 50  $\mu$ M (pg 23, lines 6-19). The specification states ES cells propagated in PD098059 remain pluripotent (pg 24, line 9); however, the statement is based on an experiment in which ZIN40 ES cells were treated with PD098059 with or without LIF. The specification teaches using IOUD2 ES cells, which carry a  $\beta$ geo gene in the oct-4 locus. The structure and function of the IOUD2 ES cells cannot be determined; it is unclear if  $\beta$ geo is expressed under the control of the oct-4 promoter or if the  $\beta$ geo gene replaces the oct-4 gene. No correlation between the genetically altered ES described in the examples and normal ES cells is provided.

Overall, the claims are not enabled because the specification does not teach the starting material used in the assays described. Without knowledge as to the structure and function of the genetically altered ES cells used in the assays, one of skill would not know how to repeat the results. The specification does not correlate the genetically altered ES cells to any other ES cells so that one of skill would expect the culture conditions used in the examples to cause the same effect in any other ES cells. The specification does not teach PD098059 inhibits propagation or survival of cells other than ES cells as claimed. It would require one of skill undue experimentation to determine how to perform the method described in the examples because the structure and function of the genetically altered ES cells is not taught. It would require one of skill undue experimentation to determine how to promote propagation/survival of ES cells

and inhibit propagation of other cells as claimed using the teachings in the specification, specifically in the examples, because the specification does not correlate the results obtained in genetically altered ES cells of unknown structure and function to ES cells known in the art.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12, 14-21, 25-28, 30-39, 43, 44 and 46-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of the compounds present in the ES culture claimed cannot be determined (claim 12). It is unclear if the first and second compound may be the same or if they must be different. The metes and bounds of compounds that "promote propagation or survival of ES cells" cannot be determined. It is unclear if compounds found in media such as dNTPs are encompassed by the phrase or if the phrase is limited to growth factors that stimulate ES cell propagation/survival specifically. The metes and bounds of compounds that "inhibit propagation or survival of cells other than ES cells" cannot be determined because the specification and the art at the time of filing did not teach any such compounds. The distinction between "propagation" and "survival" cannot be determined. Overall, the reagents required for the method cannot be determined.

The metes and bounds of compounds that "selectively inhibit" cannot be determined (claim 14, 19). It cannot be determined how the term "selectively" describes how the compound inhibits.

The metes and bounds of signaling pathways that are "essential" to propagation or survival of cells other than ES cells cannot be determined (claim 14, 30). Those pathways that are "essential" to propagation or survival of cells other than ES cells are not defined in the specification or the art at the time of filing.

Cytokines that "activate gp130" cannot be determined (claim 16, 21, 32). It is unclear if LIF is encompassed by the phrase. It is unclear if cytokines other than LIF are encompassed by the phrase.

The metes and bounds of the compounds present in the composition for culturing ES cells cannot be determined (claim 18). It is unclear if the first and second compound may be the same or if they must be different. The metes and bounds of compounds that "inhibit differentiation of ES cells" cannot be determined. The metes and bounds of compounds that "inhibit propagation or survival of cells other than ES cells" cannot be determined because the specification and the art at the time of filing did not teach any such compounds. The distinction between "propagation" and "survival" cannot be determined. Overall, the reagents required for the composition cannot be determined.

The metes and bounds of the compounds present in the ES cell culture medium cannot be determined (claims 25, 26, 28). It is unclear if the first and second compound may be the same or if they must be different. The metes and bounds of compounds that "promote proliferation of ES cells" (25, 28), that enhance the response of ES cells

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to the first compound (25), that act "through a cell-surface receptor and exerts its activity through at least one receptor subunit" (26), that "modifies an intracellular signaling pathway so as to increase the response of the S cell to the first compound" (26) or that "inhibit propagation or survival of cells other than ES cells" cannot be determined because the specification and the art at the time of filing did not teach any such compounds. The distinction between "propagation" and "survival" cannot be determined. Overall, the reagents required for the culture medium cannot be determined.

The metes and bounds of the method of culturing ES cells (claim 34, 37, 43) cannot be determined. The metes and bounds of compounds that selectively inhibits propagation or survival of cells other than ES cells cannot be determined (claim 34, 37). The structure of cells expressing a compound that selectively promotes self-renewal of ES cells, inhibits propagation or survival of cells other than ES cells or both cannot be envisioned (43). The metes and bounds of compounds that "promote self-renewal of ES cells" cannot be determined (43). The metes and bounds of compounds that "inhibit propagation or survival of cells other than ES cells" cannot be determined because the specification and the art at the time of filing did not teach any such compounds (43). The distinction between "propagation" and "survival" cannot be determined. It is unclear if genetic alteration is encompassed by the claim, and if so, is the cell genetically altered to express PG098059? Overall, the reagents required for expressing a compound in a cell having those functions cannot be determined and are not clearly set forth.



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Claim 35 is wholly unclear. It cannot be determined which cells are dissociated. The phrase "in the presence of the or a further compound" does not make sense.

The metes and bounds of "primitive" endoderm cannot be determined (38). It is unclear if any endoderm is primitive or if the phrase is limited to endoderm that exists during a specific time during development.

Dependent claims 14-17, 19-21, 26-28, 30-33, 35, 36, 38, 39, 44, 46-50 are indefinite because they begin with "A...." Dependent claims should refer to –The method of claim 12... -- or –The composition of claim 18—to be clear.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 12, 14-21, 25-28, 30-39, 43, 44 and 46-50 are rejected under 35 U.S.C. 102(a) as being anticipated by Niwa of record (July 1, 1998, Genes & Development, Vol. 12, pg 2048-2060).

Niwa taught PD098059 blocked activation of the ERK kinases but does not inhibit ES cell colony formation in response to LIF (pg 2056, col. 1, 7 lines from the bottom). Thus, Niwa cultured ES cells in PD098059 and LIF, which inherently has all the effects, claimed.

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**Conclusion**

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of formal matters can be directed to the patent analyst, Dianiece Jacobs, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-3388.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael C. Wilson



**MICHAEL WILSON  
PRIMARY EXAMINER**